UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/258,216	02/26/99	SODERLUND	H 04990.0043.U

HM22/0813

DAVID A. KALOW, ESQ.
KALOW, SPRINGUT & BRESSLER LLP
488 MADISON AVENUE,
19TH FLOOR
NEW YORK NY 10022

EXAMINER	
ARTHUR, L	
ART UNIT	**PAPER NUMBER**
1655	11

DATE MAILED: 08/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/258,216	Sonderlund et al.
Examiner	**Art Unit**
Lisa Athur	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on May 21, 2001

2a) [X] This action is FINAL. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) 40-81 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) 40-81 is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirem

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [ ] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

1. This action is in response to the paper filed May 21, 2001. Claims 1-39 have been canceled and claims 40-81 have been newly added. All of the amendments and arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. Any rejections which have not been reiterated have been withdrawn as being obviated by the claim amendments. This action contains new grounds of rejection which have been necessitated by the amendments made to the claims. This action is FINAL.

NEW GROUNDS OF REJECTION

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 40-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 40- 50, 61-71 are indefinite over the recitation in step (d) of "the labeling moiety at the 3' end" because this phrase lacks antecedent basis. Step © recites that a "detectable primer extension product comprising a labeling moiety is formed" but does not recite that the labeling moiety is at the 3' end of the primer extension product. Consequently, the claims are not

clear as to whether these two labeled primer extension products are the same or different reagents.

B) Claims 51-60 are indefinite over the recitation in step (d) of "which differs depending upon whether the chain terminating nucleotide analogue is complementary or not complementary to the defined site". This phrase makes the claims unclear because it does not clearly set forth how or from what the "detectable primer extension product" "differs".

C) Claims 61-71 are further indefinite over the recitation in step © of the phrase "none of the chain terminating nucleotide analogues are not complementary to the defined site" because this phrase contains a double negative which renders the claims unclear. That is, the claims are unclear as to whether they are intended to mean that all of the chain terminators are not complementary or that all of the chain terminators are complementary.

D) Claims 72-81 are indefinite over the recitation of the phrase "which differs depending upon whether one of the chain terminating nucleotide analogues is complementary to the defined site or none of the chain terminating nucleotide analogues is complementary to the defined site". This phrase makes the claims unclear because it does not clearly set forth how or from what the "detectable primer extension product" "differs".

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 40-81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 40-81 are not supported by the specification for the reasons that follow, and therefore introduce new matter into this claims. Claims 40-50 are drawn to a method of identifying a nucleotide at a defined site by hybridizing a primer whose 3' end binds to a nucleotide flanking the nucleotide to be detected and extending the primer in the presence of at least one deoxynucleotide and a chain terminating nucleotide to form a detectable extension product containing a labeling moiety if the chain terminator is not complementary to the specific nucleotide to be identified. Claims 51-60 are drawn to a the same method wherein the primer is extended in the presence of at least one deoxynucleotide and a chain terminating nucleotide analogue such that a detectable product is formed which differs depending upon whether or not the chain terminating nucleotide is complementary to the defined site. Claims 61-71 are drawn to the same method wherein primer extension is performed in the presence of at least one deoxynucleotide and more than one chain terminating nucleotide analogue such that a detectable primer extension product comprising a labeling moiety is formed if [none of] the chain terminators are not complementary to the defined site. Claims 72-81 are drawn to the same method wherein primer extension occurs in the presence of at least one deoxynucleotide and more than one chain

terminator such that the primer extension product differs depending upon whether or not the one chain terminating nucleotide is complementary to the defined site or whether none of the chain terminators are complementary.

However, a thorough review of the specification reveals that the specification does not describe such methods. Specifically, the specification teaches that the method uses labeled nucleotides which match the variable nucleotide to detect the variable nucleotide in the target nucleic acid (page 7, lines 17-19 and page 10, line 4-7). Pages 10-14, line 5 of the specification describe introducing an affinity moiety into the target nucleic acid during amplification of the target nucleic acid (prior to the detection steps for the variable nucleotide) to allow immobilization of the target nucleic acid. Page 14, lines 6-28 describe the separation of the amplified target nucleic acid from the amplification mixture. Page 15 through page 16, line 11 describes the detection step primer and teaches that it can be modified to have an affinity moiety different from the affinity moiety used during amplification but the teaches that the preferred detection primer is unmodified. Pages 16, line 12 through page 17, line 19 describes the extension of the detection primer. Here the specification teaches that the nucleotide mixture may be one or more nucleoside triphosphate but induces at least one labeled or modified nucleotide which is either a labeled dNTP or a dideoxynucleotide (ddNTP). Page 17 teaches that the dNTP or DDNTP is labeled with a detectable label or modified to have an attachment moiety capable of binding to a detectable label. Page 17, line 20-page 20 teaches particular embodiments of the invention. Here the specification describes (1) a method wherein only labeled DDNTP

corresponding to the variable nucleotide is added; (2) a method wherein labeled dNTP corresponding to the variable nucleotide is added and that unlabeled ddNTP is preferably included in this embodiment; (3) a method which uses two or more different, differently labeled dNTPs corresponding to the variable nucleotide; (4) a method using a detection step primer which is -n- nucleotides away from the variable nucleotide and using unlabeled dNTPs which are complementary to the -n- nucleotides between the primer and the variable nucleotide and labeled dNTPs corresponding to the variable nucleotide which could be substituted for labeled ddNTPs; (5) a method wherein two or more variable nucleotide are identified which requires the use of at least two different detection primers that hybridize 3' of each of the variable nucleotides to be identified. Pages 21-38 describe specific examples and further exemplify labeling with radiolabels, enzyme labels and fluorescent labels.

The specification does not, however, describe a method wherein extension occurs in the presence of at least one deoxynucleotide and one or more chain terminating oligonucleotides wherein neither the deoxynucleotide nor the chain terminator is detectably labeled as is now encompassed by the claims. The specification does not teach labeling the primer extension product after the deoxynucleotide and/or the chain terminator is incorporated but such a method is now encompassed by the claims. The specification is very specific that either the deoxynucleotide or the chain terminating nucleotide analogue is labeled and the means by which the variable nucleotide is detected. The specification does not describe broadly describe the concept of forming a primer extension product which contains a label at the 3' end when the chain

terminator is not complementary to the variable nucleotide. Instead the specification teaches that a labeled deoxynucleotide is used when the chain terminator is not complementary to the variable base. The method described in the specification is directed to detecting nucleotides of known sequence so the base on the deoxynucleotides and the chain terminators for use in the method is predetermined. Consequently, whether or not the deoxynucleotide or the chain terminator will hybridize to the defined site is also predetermined. The specification is clear that either the deoxynucleotide or the chain terminator is labeled (directly or indirectly) in this method. Consequently, the specification does not support the method of claims 40-81 which recite the primer is extended in the presence of a deoxynucleotide of chain terminator which may or may not be labeled.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-11 and 34-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of U.S. Patent No. 6,013,431. Although the conflicting claims are not identical, they are not patentably distinct from

each other because the claims of this application and the patent contain overlapping subject matter. The claims of patent 6,013,431 are drawn to a method for determining a nucleotide variation at a defined site using a primer which hybridizes at its 3' end to the nucleotide flanking the nucleotide variation and extending in the presence of a mixture containing at least one labeled deoxynucleotide and at least one dideoxynucleotide. The instant claims are more broadly drawn to the same method wherein extension occurs in the presence of a mixture containing at one deoxynucleotide and one or more than one chain terminating nucleotide analogue wherein the deoxynucleotide or the chain terminator may or may not be labeled. Because the claims of the patent and the instant claims are both include a method wherein the deoxynucleotide is labeled, the claims of the patent and the instant claims contain overlapping subject matter.

8. No claims are allowable.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Monday-Wednesday from 7:00 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800 | 600

August 11, 2001